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(FILE 'HOME' ENTERED AT 14:24:02 ON 25 OCT 2005)

FILE 'MEDLINE, CANCERLIT, AGRICOLA, CAPLUS, SCISEARCH' ENTERED AT  
14:24:56 ON 25 OCT 2005

L1 252036 S ARTHRITIS  
L2 12735 S LENTIVIR?  
L3 655 S IRAP  
L4 0 S L1 (L) L2 (L) L3  
L5 700 S L1 (L) L2  
L6 330 DUP REM L5 (370 DUPLICATES REMOVED)  
L7 12056 S INTERLEUKIN? (5W) RECEPTOR (5W)ANTAGONIST  
L8 9 S L1 (L) L2 (L) L7  
L9 5 DUP REM L8 (4 DUPLICATES REMOVED)  
L10 5 SORT L9 PY

FILE 'STNGUIDE' ENTERED AT 14:29:45 ON 25 OCT 2005

FILE 'MEDLINE, CANCERLIT, AGRICOLA, CAPLUS, SCISEARCH' ENTERED AT  
14:38:42 ON 25 OCT 2005

L11 107527 S GENE THERAPY  
L12 26 S L1 (L) L11 (L) L2  
L13 15 DUP REM L12 (11 DUPLICATES REMOVED)  
L14 15 SORT L13 PY  
E PAWLIUK? ROBERT?/AU  
L15 2 S E1  
E LEBOULCH PHILIPPE/AU  
L16 185 S E2  
L17 102 S E3  
L18 288 S L15 OR L16 OR L17  
L19 9 S L18 AND L1  
L20 5 DUP REM L19 (4 DUPLICATES REMOVED)  
L21 5 SORT L20 PY

=> d an ti so au ab pi l21 1-5

L21 ANSWER 1 OF 5 MEDLINE on STN  
AN 2002211466 MEDLINE  
TI In vivo gene delivery to synovium by lentiviral vectors.  
SO Molecular therapy : journal of the American Society of Gene Therapy, (2002  
Apr) 5 (4) 397-404.  
Journal code: 100890581. ISSN: 1525-0016.  
AU Gouze Elvire; Pawliuk Robert; Pilapil Carmencita; Gouze Jean-Noel; Fleet  
Christina; Palmer Glyn D; Evans Christopher H; **Leboulch Philippe**  
; Ghivizzani Steven C  
AB The delivery of anti-arthritic genes to the synovial lining of joints is  
being explored as a strategy for the treatment of rheumatoid  
**arthritis**. In this study, we have investigated the use of VSV-G  
pseudotyped, HIV-1-based lentiviral vectors for gene delivery to articular  
tissues. Recombinant lentivirus containing a beta-galactosidase/neomycin  
resistance fusion gene under control of the elongation factor (EF) 1alpha  
promoter efficiently transduced human and rat synoviocytes and  
chondrocytes in cell culture. When directly injected into the knees of  
rats, this vector transduced synovial lining cells, but not other  
articular tissues such as cartilage. We also constructed a lentiviral  
vector containing the human interleukin-1 receptor antagonist (IL1RA) cDNA  
and examined transgene expression in vitro and in vivo following injection  
into the knee joints of rats. In immunocompetent animals, intra-articular  
IL1RA expression was high and persisted, at a sharply declining rate, for  
approximately 20 days. In immunocompromised rats, however,  
lentivirus-mediated intra-articular expression of human IL1RA was found to  
persist for at least 6 weeks. Extra-articular expression of the transgene  
was minimal. These results indicate that lentiviral vectors are capable  
of efficient in vivo gene transfer to synovium and merit further  
investigation as a means of providing long-term expression for gene-based  
treatments of **arthritis**.

L21 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:813886 CAPLUS  
 DN 137:320303  
 TI Method of treating **arthritis** using lentiviral vectors in gene therapy  
 SO PCT Int. Appl., 51 pp.  
 CODEN: PIXXD2  
 IN Pawliuk, Robert; Leboulch, Philippe  
 AB Novel methods for treating and preventing **arthritis**, such as rheumatoid **arthritis**, are disclosed which employ lentiviral gene delivery vectors, including HIV-based lentiviral vectors, to deliver a therapeutic gene to a subject. Lentiviral-based vectors treat **arthritis** by promoting high-level expression of the transferred therapeutic gene in the target tissue of the subject. High-titer VSV-G pseudotyped HIV-1-based lentiviral vectors were evaluated for their ability to deliver exogenous genes to articular tissues. Expression of hIL-1Ra via lentiviral injection reduced inflammation of the knee (site of injection) in **arthritis** induced rats compared to control animals.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083080	A2	20021024	WO 2002-US8600	20020319
WO 2002083080	A3	20030220		
WO 2002083080	C2	20030703		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

L21 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:813857 CAPLUS  
 DN 137:320302  
 TI Method of treating **arthritis** using lentiviral vectors in gene therapy  
 SO PCT Int. Appl., 54 pp.  
 CODEN: PIXXD2  
 IN Pawliuk, Robert; Leboulch, Philippe  
 AB Novel methods for treating and preventing **arthritis**, such as rheumatoid **arthritis**, are disclosed which employ lentiviral gene delivery vectors, including HIV-based lentiviral vectors, to deliver a therapeutic gene to a subject. Lentiviral-based vectors treat **arthritis** by promoting high-level expression of the transferred therapeutic gene in the target tissue of the subject. High-titer VSV-G pseudotyped HIV-1-based lentiviral vectors were evaluated for their ability to deliver exogenous genes to articular tissues. Expression of hIL-1Ra via lentiviral injection reduced inflammation of the knee (site of injection) in **arthritis** induced rats compared to control animals.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002082908	A1	20021024	WO 2002-US8711	20020321
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004241141	A1	20041202	US 2003-688780	20031015

L21 ANSWER 4 OF 5 MEDLINE on STN

AN 2003206924 MEDLINE

TI Lentiviral-mediated gene delivery to synovium: potent intra-articular expression with amplification by inflammation.

SO Molecular therapy : journal of the American Society of Gene Therapy, (2003 Apr) 7 (4) 460-6.  
Journal code: 100890581. ISSN: 1525-0016.

AU Gouze Elvire; Pawliuk Robert; Gouze Jean-Noel; Pilapil Carmencita; Fleet Christina; Palmer Glyn D; Evans Christopher H; **Leboulch Philippe**; Ghivizzani Steven C

AB Clinical translation of gene-based therapies for arthritis could be accelerated by vectors capable of efficient intra-articular gene delivery and long-term transgene expression. Previously, we have shown that lentiviral vectors transduce rat synovium efficiently in vivo. Here, we evaluated the functional capacity of transgene expression provided by lentiviral-mediated gene delivery to the joint. To do this, we measured the ability of a lentiviral vector containing the cDNA for human interleukin-1 receptor antagonist (LV-hIL-1Ra) to suppress intra-articular responses to IL-1beta. Groups of rats were injected in one knee with 5 x 10(7) infectious units of LV-IL-1Ra. After 24 h, a range of doses of fibroblasts (3 x 10(3), 10(4), 3 x 10(4), or 10(5) cells) genetically modified to overexpress IL-1beta was injected into both knees. Intra-articular delivery of LV-hIL-1Ra strongly prevented swelling in all treated knees, even in those receiving the greatest dose of IL-1beta(+) cells. Cellular infiltration, cartilage erosion, and invasiveness of inflamed synovium were effectively prevented in LV-hIL-1Ra-treated knees and were significantly inhibited in contralateral joints. Beneficial effects were also observed systemically in the lentivirus-treated animals. Interestingly, intra-articular expression of the IL-1Ra transgene was found to increase in relation to the number of IL-1beta(+) cells injected. Further experiments using GFP suggest this is due to the proliferation of cells, stably modified by the integrative lentivirus, in response to inflammatory stimulation.

L21 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:591418 CAPLUS

DN 139:111671

TI Heterodimer formation-based method using PLGF gene or VEGF-B gene delivery for inhibiting angiogenesis

SO PCT Int. Appl., 17 pp.

CODEN: PIXXD2

IN Cao, Yihai; Cao, Renhai; Pawliuk, Robert; **Leboulch, Philippe**

AB Methods for inhibiting angiogenesis using gene therapy are disclosed. Genes encoding PLGF or VEGF-B are delivered to cells e.g., tumor cells, which express VEGF, such that heterodimers of PLGF/VEGF and/or VEGF-B/VEGF are formed within the cells, preferably at a greater ratio than homodimers of VEGF/VEGF. The heterodimers have reduced angiogenic activity compared to VEGF homodimers.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062788	A2	20030731	WO 2003-US1360	20030117
WO 2003062788	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004062751	A1	20040401	US 2003-346589	20030117

L14 ANSWER 10 OF 15 MEDLINE on STN

AN 2003304037 MEDLINE

TI Gene transfer as a future therapy for rheumatoid arthritis.

SO Expert opinion on biological therapy, (2003 Jul) 3 (4) 587-98. Ref: 103  
Journal code: 101125414. ISSN: 1471-2598.

AU Muller-Ladner Ulf; Pap Thomas; Gay Renate E; Gay Steffen

AB Inhibiting key pathogenic processes within the rheumatoid synovium is a most attractive goal to achieve, and the number of potential intra- and extracellular pathways operative in rheumatoid arthritis (RA) that could be used for a **gene therapy** strategy is increasing continuously. Gene transfer or **gene therapy** might also be one of the approaches to solve the problem of long-term expression of therapeutic genes, in order to replace the frequent application of recombinant proteins, in the future. However, at present, **gene therapy** has not reached a realistic clinical stage, which is mainly due to severe side effects in humans, the complexity of RA pathophysiology and the current state of available gene transfer techniques. On the other hand, novel gene delivery systems are not restricted to vectors or certain types of cells, as mobile cells including macrophages, dendritic cells, lymphocytes and multipotent stem cells can also be used as smart gene transfer vehicles. Moreover, the observation in animal models that application of viral vectors into a joint can exert additional therapeutic effects in nearby joints might also facilitate the transfer from animal to human **gene therapy**. Future strategies will also examine the potential of novel long-term expression vectors such as **lentiviruses** and cytomegalovirus (CMV)-based viruses as a basis for future clinical trials in RA.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L27	1	10/688,780	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 13:49
L28	10	Pawliuk Robert	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 13:49
L29	32	Leboulch Philippe	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 13:49
L30	78402	arthritis	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 13:50
L32	3	I28 and I30	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 13:50
L33	4	I29 and I30	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 13:50
L34	5387	lentivir\$3	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 13:51
L35	1934	I30 and I34	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 14:01
L36	27	(I30 and I34).clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 13:51
L37	579	lentivir\$3.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 13:51
L38	178	I37 and I30	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 14:21
L40	449	((arthritis SAME gene SAME therap\$5) and (Interleukin WITH receptor)) and (vector or viral or virus or lentiviral)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 14:10
L41	322	((((arthritis SAME gene SAME therap\$5) and (Interleukin WITH receptor)) and (vector or viral or virus or lentiviral)) and (synovial or joint)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 13:59

L42	25	Glorioso Joseph	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 14:00
L45	130	I35 and I40	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 14:02
L46	98	I35 and I41	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/10/25 14:02
L47	881	(Interleukin WITH receptor) and I34	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 14:10
L48	591	I47 and I30	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 14:10
L49	14	(Interleukin WITH receptor).clm. and I48	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 14:11
L50	21	(US-20040241141-\$).did. or (US-5858355-\$ or US-5986059-\$ or US-6004942-\$ or US-6018029-\$ or US-6063600-\$ or US-6156887-\$ or US-6159464-\$ or US-6204371-\$ or US-6306820-\$ or US-6413511-\$ or US-6818209-\$).did. or (WO-2082908-\$ or WO-9211359-\$).did. or (JP-2000209980-\$).did. or (WO-9211359-\$ or US-5747072-\$ or US-6018029-\$ or WO-200126675-\$ or WO-200282908-\$ or WO-200283080-\$).did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 14:15
L51	5	I50 and I34	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 14:18
L52	5	I50 and (I30 and I34)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/10/25 14:19
L53	1	IRAP I34	US-PGPUB; USPAT; EPO; JPO; DERWENT	SAME	ON	2005/10/25 14:20
L54	17	IRAP I34	US-PGPUB; USPAT; EPO; JPO; DERWENT	AND	ON	2005/10/25 14:21
L56	13	I37 I30	US-PGPUB; USPAT; EPO; JPO; DERWENT	SAME	ON	2005/10/25 14:21